TABLE 4: GP IIb / IIIa INHIBITORS AS ADJUNCTIVE TREATMENT TO THROMBOLYTIC THERAPY IN ACUTE MYOCARDIAL INFARCTION

TRIAL	DRUG	N	INCLUSION CRITERIA	PATIENT SUMMARY	OUTCOME
TAMI 8 [117]	$m7E_3$ FAB	70	Patients 18-76 yrs < 6hrs of AMI onset with: ST segment elevation ≥ 0.1mV in 2 contiguous leads or in the presence of LBBB, had primary ST segment changes in the inferior or anterior leads.	10 to control; 60 to $m7E_3$ Fab (increasing doses). All received 100mg of rt.-PA (60mg in 1 hr + 20mg for each subsequent 2 hrs). All received aspirin and heparin. Angiogram and revascularisation only performed if clinically indicated. Angiogram performed in 9 control and in 34 $m7E_3$Fab treated patients.	Incidence of recurrent ischaemic events was similar in both groups (2/10 vs 8/60 for $m7E_3$Fab). 56% controls had culprit artery patency on angiogram vs 92% in $m7E_3$Fab treated patients.
IMPACT-AMI [118]	EPTIFIBATIDE	180	Patients 18-65 yrs (18-75 yrs in Grp 2) < 6hrs of AMI onset with: 1. ST segment depression in leads V1-V6 consistent with posterior current of injury. 2. ST segment elevation ≥ 0.1mV in 2 inferior or anterior leads or in leads I and aVL or primary ST segment change in inferior or anterior leads with LBBB.	Randomised to Group 1 (increasing doses of integrilin or placebo bolus and continuous infusion) or Group 2 (highest dose of integrilin in grp 1 or placebo). All received up to 100mg wt adjusted accelerated alteplase. Integrilin given between 10 – 30 mins after initiation of alteplase. All received aspirin 325mg and heparin IV (APTT 2-2.5 the control). All had 90 min coronary angiography.	Primary end point of TIMI 3 flow: 66% in highest dose eptifibatide treated patients vs 39% for placebo (p=0.006). The groups had similar rates of composite end point (42% placebo vs 43% for highest dose eptifibatide treated patients) of death, reinfarction, stroke, percutaneous or surgical coronary revascularisation, or new in-hospital heart failure or pulmonary oedema.
PARADIGM [119]	LAMIFIBAN	353	Patients 21-75 yrs < 12 hrs of AMI onset with: ST segment elevation ≥ 1mm in 2 limb leads or ≥ 2mm in 2 contiguous precordial leads to be eligible for thrombolytic therapy.	Three parts: A, B and C. A: Patients received open labelled low dose (n=15) and high dose (n=15) lamifiban. B: Patients randomised to lamifiban (n=112) or placebo (n=61) bolus and infusion for 24 hrs. C: Patients randomised to lamifiban (N=94) or placebo (N=56) bolus and infusion for 48 hrs. At investigators discretion, patients received either wt adjusted accelerated rt.-PA (100mg / 90 mins; n=266) or streptokinase (1.5 million IU / 1 hr; n=85). All received aspirin and heparin. Only 34 patients had the 90 min angiogram. 246/353 had angiogram during the hospitalisation.	No significant reduction in the primary efficacy outcome of angiographic, continuous ECG and clinical markers of reperfusion failure by hospital discharge or 30 days was observed with placebo and lamifiban. Platelet aggregation was inhibited in a dose dependent manner. 62.5% of placebo vs 80.1% of lamifiban group showed ECG evidence of reperfusion at 90 mins (p=0.005).

TRIAL	DRUG	N	INCLUSION CRITERIA	PATIENT SUMMARY	OUTCOME
TIMI 14 [120]	ABCIXIMAB	888	Patients 18-75 yrs with < 12 hrs of AMI onset with: ST segment elevation ≥ 0.1 mV in 2 contiguous ECG leads.	Two phases: Dose Finding (n=677) and Dose Confirmatory phases (n=211). During the Dose Finding Phase – alteplase 20 – 100mgs, streptokinase 500 – 1500 $Ux10^3$ and abciximab 0.25 or 0.30 mg/kg bolus followed by infusion of 0.125µg/kg/min for 12hrs. During the Dose Confirmatory Phase – alteplase 50-100mgs and abciximab 0.25mg/kg bolus followed by 0.125µg/kg/min for 12hrs with either low dose or very low dose heparin. All received aspirin and heparin (except streptokinase at 1500 $Ux10^3$) 408 patients had evaluable angiogram at 60 mins and 791 patients at 90 mins.	From the pooled data TIMI 3 flow: 60 mins - 43% alteplase only group vs 72% (50mg alteplase + abciximab group) (p=0.0009). 90 mins - 62% alteplase only group vs 77% (50mg alteplase + abciximab group) (p=0.01). No major differences were seen for the overall rates of mortality, recurrent MI and development of severe pump failure across the groups.
SPEED [121]	ABCIXIMAB	351	Patients ≥ 18 yrs with AMI < 6 hrs with: 1. ST segment elevation ≥ 1mm in 2 contiguous ECG leads. 2. Eligible for PCI	Patients were randomised to r-PA (10+10U), r-PA (5+5U) + abciximab or abxicimab alone. Abciximab dose: 0.25mg/kg bolus + 0.125µg/kg/min for 12 hrs. All received aspirin and heparin. All had coronary angiography at 60 to 90 mins	TIMI 3 flow at 60-90 mins: 48% r-PA vs 62% r-PA + abxicimab vs 29% abciximab alone.
INTRO AMI [122]	EPTIFIBATIDE	342	Patients ≥ 18 yrs with AMI < 6 hrs with: 1. ST segment elevation ≥ 1mm in 2 limb leads. Or 2. ST segment elevation ≥ 2mm in 2 contiguous precordial leads. Or 3. Primary ST change in inferior or anterior leads with LBBB.	Patients were randomised into 8 different groups. All patients received low dose rt.-PA (25mg or 50mg) and eptifibatide (180µg/kg bolus or 180/90 µg/kg double bolus 30 mins apart, with infusion regimen of either 1.33 or 2.0 µg/kg/min). All patients received aspirin and heparin.	Maximum TIMI 3 flow at 60 and 90 mins observed for combination of low dose rt.-PA (50mg) with double bolus eptifibatide (180/90 + 1.33 µg/kg/min infusion) - 65% and 78% respectively.

AMI = Acute myocardial infarction; ECG = Electrocardiogram; LBBB = Left bundle branch block
rt.-PA = Recombinant tissue plasminogen activator/Alteplase; r-PA = Reteplase; PCI = Percutaneous coronary intervention